CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA
Methiocarb

Chemical Code # 000375, Tolerance # 00320
SB 950 # 011

March 25, 2003

I. DATA GAP STATUS

Chronic toxicity, rat:	Data gap, inadequate study, no adverse effect indicated
Chronic toxicity, dog:	No data gap, acceptable study, no adverse effect.
Oncogenicity, rat:	No data gap, acceptable study, no adverse effect.
Oncogenicity, mouse:	Data gap, inadequate study, no adverse effect indicated.
Reproduction, rat:	No data gap, acceptable study, no adverse effect
Teratology, rat:	No data gap, acceptable study, no adverse effect.
Teratology, rabbit:	No data gap, acceptable study, no adverse effect.
Teratology, rabbit (dermal)	No data gap, acceptable study, possible adverse effect.
Gene mutation:	No data gap, acceptable study, no adverse effect.
Chromosome effects:	No data gap, acceptable study, no adverse effect.
DNA damage:	No data gap, acceptable study, no adverse effect.
Neurotoxicity:	Not required at this time

Toxicology one-liners are attached.

All record numbers through 202784 and 944422 were examined.
** indicates an acceptable study.
Bold face indicates a possible adverse effect.

File name: T030325
Compiled by: Silva, 3/25/03

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

COMBINED, RAT

No study on file.

CHRONIC TOXICITY, RAT

320 - 005 944403 "Chronic Oral Toxicity of Bay 37344 to Rats", (Doull, J., Root, M., Meskauskas, J.; Toxicity Laboratory, University of Chicago, Chicago, IL; Report # 21791, 12/15/67). Bay 37344 technical (methiocarb, purity not stated) was fed in diet to Sprague-Dawley rats (24/sex/dose) at 0 (Rockland Rat Diet), 25, 50, and 100 ppm for 20 months. Chronic NOEL = 100 ppm (There were no treatment-related effects at any dose.) ChE NOEL = 100 ppm (There were no treatment-related effects at any dose.) Not acceptable and not upgradeable (An MTD was not achieved. Hematology, urinalysis and ophthalmology were not performed. Serum chemistry, necropsy, and histopathology were incomplete. Individual data are not provided. Test article and dosing material characteristics and analyses were not included. Chronic pneumonia was noted in all groups and low 18 month survival was recorded in males.) No adverse effect indicated. (J. Christopher, 2/15/85; updated to electronic format, Green & Silva, 3/5/03).

SUBCHRONIC (DERMAL), RABBIT

** 320 - 144 071863 "A 21-Day Dermal Toxicity Study of MESUROL Technical in Albino Rabbits," (Proctor, B.G.; Bio-Research Laboratories LTD, Senneville, Quebec, Canada; Bio-Research Laboratory #: 51901; Mobay Report #: 98369; 11/23/88). Mesurol technical (methiocarb, 99.3% pure) was administered dermally (with occlusion) to New Zealand White rabbits (5/sex/dose) at 0 (saline 0.9%), 60, 150 and 375 mg/kg for 21 days (6 hours/day). NOEL = 150 mg/kg (There were intermittent statistically significant decreases in food consumption in males at 375 mg/kg. At 375 mg/kg on day 0 (before treatment initiation), PChE was 8% lower than controls in males. Day 7 PChE was decreased by 22%, day 14 by 31% (statistically significant, $p < 0.05$) and day 21 by 24% (statistically significant, $p < 0.01$) in males at 375 mg/kg. Grossly at 375 mg/kg, females showed an increased incidence in depressed and dark areas of the lung. Histopathologically, at 375 mg/kg, both sexes showed an increased incidence in lung atelectasis and females at 375 mg/kg showed increased intra-alveolar hemorrhage.) Acceptable with no adverse effects. Silva, 3/13/03

** 320 - 152 096167 "A 21-Day Dermal Toxicity Study of MESUROL Technical in Albino Rabbits (Supplemental Submission)," (Proctor, B.G.; Bio-Research Laboratories LTD, Senneville, Quebec, Canada; Bio-Research Laboratory #: 51925; Mobay Report #: 98369-1; 8/31/89). This study was performed to supplement a previous study (DPR volume/record #: 320 - 144 071863) reviewed by DPR (See Summary of Toxicology Data). Mesurol technical (methiocarb, 97.5% pure) was administered dermally (with occlusion) to New Zealand White rabbits (5/sex/dose) at 0 (saline 0.9%) and 500 mg/kg for 21 days (6 hours/day). NOEL < 500 mg/kg (Female body weights were statistically significantly decreased on days 15, 19 and 21 at 500 mg/kg. There were intermittent statistically significant decreases in food consumption in both sexes at 500 mg/kg.

There was a statistically significant increase in GOT and GPT in females at 500 mg/kg at termination. PChE at 500 mg/kg in females was statistically significantly decreased (14%) on day 14. Males had increased relative and absolute right testis weights and females had decreased relative and absolute right ovary weight at 500 mg/kg. Grossly at 500 mg/kg, males showed an increased incidence in depressed areas of the lung. Histopathologically, at 500 mg/kg, males showed an increased incidence in lung atelectasis, prominent lymphoid nodules, interstitial pneumonia and ossification.) Acceptable in conjunction with DPR volume/record #: 320 - 144 071863. No adverse effects. Silva, 3/13/03

CHRONIC TOXICITY, DOG

320 - 005 944404 "Chronic Oral Toxicity of Bay 37344 to Male and Female Dogs," (Doull, J., Root, M., Meskauskas, J.; Toxicity Laboratory, University of Chicago, Chicago, IL, Report # 22115, 2/1/68). Bay 37344 (methiocarb, purity not stated) was fed in diet to Beagle dogs (2/sex/dose) at 0 (Rockland Dog Diet), 50, 100 and 250 ppm for 24 months. There were no treatment-related effects observed in this study. No adverse effects indicated. Chronic NOEL > 250 ppm. ChE NOEL > 250 ppm. The sudy is not acceptable and not upgradeable (numerous deficiencies). (J. Christopher, 2/15/85; updated to electronic format, Green & Silva, 3/3/03).

** 320 - 097, 102 010416, 027103 "Chronic Toxicity Study in Dogs (Two-Year Feeding Experiment), Additional Data," (Hoffmann, K., Schilde, B.; Bayer AG, Institut fur Toxikologie, Wuppertal, Germany, Report # 69364, 12/4/80 (original study); 1/22/85 (additional study)). H 321 (methiocarb; 98.4% pure) was fed in diet to Beagle dogs (4/sex/dose) for 104 weeks at 0 (dog diet), 5 (reduced from 15 ppm in week 3), 60, and 240 ppm. Chronic NOEL = 60 ppm (Tremors and rear leg weakness were observed at 240 ppm). ChE NOEL = 5 ppm (Plasma ChE was inhibited at 60 and 240 ppm). The study is acceptable with deficiencies (Histopathology was incomplete (the spinal cord was not examined). The death of one low dose female during week 98 occurred. Test article and dosing material analyses and characteristics were not included.) No adverse effects. (J. Schreider, 2/15/85; updated to electronic format, Green & Silva, 3/6/03) Additional data (individual gross pathology; Summary of gross and histopathological findings (lesion incidence/sex/dose); individual necropsy results and individual organ weights) did not affect the study status. Silva, 3/14/03.

ONCOGENICITY, RAT

320 - 081 944402 "Chronic Toxicity Study on Rats (2-Year Feeding Experiment)", (Kroetlinger, F., Loeser, E., Vogel, O.; Bayer Ag, Institut Für Toxikologie, Wuppertal, Germany, Report # 69844, 7/2/81). Mesurol (98.9% technical methiocarb) was fed in diet to SPF (Wistar TNO W. 74) rats (60/sex/dose) at 0, 67, 200 and 600 ppm for 2 years. Chronic NOEL = 200 ppm (Reduced bodyweight (5 - 11% M & 5 - 8% F) were observed in both sexes, primarily in the first 2 months of the study at 600 ppm. Slight plasma cholinesterase inhibition (28% M & 25% F) was observed at 600 ppm at 105 weeks.) Oncogenicity NOEL > 600 ppm (There were no treatment-related effects at any dose.) No adverse effects indicated. Not acceptable and not upgradeable (Marginal toxicity was observed at the high dose. Incomplete serum chemistry, urinalysis, necropsy, and histopathology were performed. Ophthalmology was not performed. A summary of pathology was not presented. Tables for incidental and non-neoplastic findings were not provided. Dosing material characteristics and analyses were not provided. The certificate of

test article analysis was not included.) (J. Christopher, 2/19/85, updated to electronic format by Green & Silva, 2/24/03).

** 320 - 081, 154 944402, 093380 "Addendum to: Chronic Toxicity Study on Rats (2-Year Feeding Experiment)", (Kroetlinger, F., Loeser, E., Vogel, O (original study); Kroetlinger, F. (addendum).; Bayer Ag, Institut Für Toxikologie, Wuppertal, Germany, Report # 69844 & 69844-1; Addendum to Bayer Report #: 10039, 7/2/81 (original) & 2/16/90 (addendum)). Mesurol (98.9% technical methiocarb) was fed in diet to SPF (Wistar TNO W. 74) rats (60/sex/dose) at 0, 67, 200 and 600 ppm for 2 years. Chronic NOEL = 200 ppm (Reduced bodyweight (5 - 11% M & 5 - 8% F) were observed in both sexes, primarily in the first 2 months of the study at 600 ppm. Slight plasma cholinesterase inhibition (28% M & 25% F) was observed at 600 ppm at 105 weeks.) Oncogenicity NOEL > 600 ppm (There were no treatment-related effects at any dose.) No adverse effects indicated. This study was originally review as unacceptable and not upgradeable (Christopher, 2/19/85), however upon submission of the requested information (QA & GLP statements; individual clinical findings, individual gross & histopathology data and analyses of H321 in diet) the study has been upgraded to acceptable for oncogenicity. Silva, 3/10/03

ONCOGENICITY, MOUSE

320 - 086 010235 "Chronic Toxicity Study on Mice (2-Year Feeding Experiment)", (Kroetlinger and Janda; Bayer AG, Institut Fuer Toxikologie, Wuppertal, Germany, Report # 85950, 7/4/83). Mesurol (H 321, 98.5% pure) was fed in diet to BOR:CFW1 (SPF) mice (47 - 52/sex/dose) at 0 (pulverized rodent feed), 67, 200 and 600 ppm (approximately 14.63, 42.81 & 131.94 mg/kg/day, Males; 19.84, 57.03 & 173.28 mg/kg/day, Females) for 2 years. Chronic NOEL = 67 ppm (Males had statistically significantly increased MCH at 600 and MCHC at $\geq$ 200 ppm (12 & 24 mos). Females had increased MCHC at 600 ppm at 12 months. Both sexes had statistically significantly increased GPT at $\geq$ 200 ppm at 24 months. Plasma ChE was statistically significantly decreased in females at 200 (42%) and 600 ppm (34%) at month 1. This was reversed by 12 months and there were no treatment-related ChE effects in brain. Body weights in females were statistically significantly decreased at 12 months at 600 ppm (10%). Absolute female spleen weights were statistically significantly decreased at 24 months at 600 ppm. Relative female heart weights were statistically significantly increased at 600 ppm at 12 months.) Oncogenicity NOEL > 600 ppm (There were no treatment-related oncogenic effects at any dose.) No adverse effect indicated. Unacceptable, not upgradeable (numerous deficiencies). (J. Christopher, 2/13/85, updated to electronic format, Green & Silva, 1/26/03)

320 - 095 010412 This volume is an exact duplicate of 320 - 086 010235, reviewed above.

REPRODUCTION, RAT

** 320 - 179 202783 "H 321 (Methiocarb): Two-Generation Study In Wistar Rats," (Eiben, R., Bach, U., Popp, A.; Bayer AG, Institute of Toxicology, Rodent Studies & Genotoxicity, Wuppertal, Germany; Report # PH31760; 1/7/02). H 321 (methiocarb, purity of 3 batches = 99.1, 99.1, 99.2%), was fed in diet to Wistar Hsd Cpb: WU (25/sex/dose) at 0, 50, 150 and 500 ppm (approximately M: 4.3, 12.5 and 41 mg/kg, F: 5.5, 15.4 and 52.1 mg/kg) from premating of F1

generation through weaning of F2 pups (2 matings of F1 parents). Parental NOEL = 50 ppm (There was a statistically significant decrease in body weights and lower food consumption for F0 males at 500 ppm. F0 females had a transitory decrease in body weights at 500 ppm. There was a statistically significant decrease in absolute and relative F0 male liver weights and increase in relative testes weights at 500 ppm. F1 females had statistically significantly decreased body weights at ≥ 150 ppm during both F2a & F2b lactations. There was a statistically significant increase in F1 parental male relative brain and pituitary weights at 500 ppm. The lactation index was low at 500 ppm (not statistically significant). Subsequently, a second mating for F1 parents was carried out. The lactation index after the 2nd mating was no different from control.) ChE NOEL = 150 ppm (There was a statistically significant decrease (23%) in plasma ChE in F0 females at 500 ppm. Plasma ChE was statistically significant decreased (17% males; 37% females) in F1 parents at 500 ppm.) Reproductive NOEL > 500 ppm (There were no treatment-related effects at any dose.) Pup NOEL = 150 ppm (There was a statistically significant decrease in F1 pup absolute thymus weights for both sexes at 500 ppm. There was a statistically significant decrease in F1 litter size at 500 ppm. F2a pups at 500 ppm had increased incidence in food pasted noses and/or mouths and more pups exhibited an empty stomach and/or intestine than controls, along with slightly lower body weights.) Acceptable. No adverse effect. Silva, 3/20/03

320 - 082 944417 "Generation Studies on Rats," (Eckhard Loser, Farbenfabriken Bayer AG, Institut fur toxikologie, Wuppertal-Elberfeld, Germany; Report # 28193, 7/10/70). Bay 37 344 (methiocarb, purity not provided), was fed in diet to FB 30 Elberfeld rats (10 males & 20 females/sex/dose) at 0 (Sniff powder feed), 30, 100, and 300 ppm. Treatment began 10 weeks prior to mating of the F0 generation and continued through 3 generations (2 litters/generation). Reproductive NOEL > 300 ppm (There were no treatment-related reproductive effects at any dose.) Systemic NOEL = 300 ppm (There were no treatment-related effects at any dose.) Pup NOEL = 100 ppm (Pup body weights at 300 ppm were statistically significantly decreased in the F2b and F3b pups throughout lactation.) No adverse effect indicated. Unacceptable and not upgradeable (dosing rationale, too few animals per group and numerous deficiencies that preclude acceptability). (J. Schreider, 2/14/85; updated to electronic format Green & Silva, 2/21/03).

320 - 079 944413 This volume is an exact duplicate of 320 - 082 944417.

TERATOLOGY, RAT

** 320 - 180 202784 "Technical Grade Methiocarb (Mesurol®): A Prenatal Developmental Toxicity Study in Wistar Rat," (Young, A.D.; Bayer Corporation, Agricultural Division, Kansas City, MO; Laboratory Project Study ID: 01-T12-DV; 1/18/02). Mesurol technical (methiocarb; 98.4% pure) was administered by gavage to mated Wistar Hanover (Crl:WI(HAN)) rats (30/dose) at 0 (0.5% CMC/0.4% Tween 80 in deionized water), 0.5, 1.5 and 5 mg/kg/day on gestation days 6 through 19. Maternal NOEL = 0.5 mg/kg/day (There was an increased incidence in clinical signs and effects observed from necropsy at ≥ 1.5 mg/kg (muscle fasciculations). There was a decrease in actual body weight gain (12.5% not statistically significant) and food consumption (11% not statistically significant) during GD 6 - 10 at 5.0 mg/kg.) Developmental NOEL = 5.0 mg/kg/day (There were no treatment-related effects at any dose.) Acceptable. No adverse effect. Silva, 3/25/03.

320 - 082 944407 "Studies on Rats for Embryotoxic and Teratogenic Effects", (Lorke, D., Farbenfabriken Bayer AG, Institut fur Toxikologie, Wuppertal-Elberfeld, Germany, Report # 32142, 11/30/71). Bay 37 344 (methiocarb; 98.9% pure) was administered by gavage to mated FB 30 females rats (19 or 20/dose) at 0 (1% tragacanth suspension), 1, 3, and 10 mg/kg/day on gestation days 6 through 15. Maternal NOEL = 3 mg/kg/day (There was decreased body weight

gain at 10 mg/kg/day.) Developmental NOEL = 10 mg/kg/day (There were no treatment-related effects at any dose.) Not acceptable and not upgradeable (Methiocarb technical and dosing solution characterizations were not included in the report. Randomization process was unclear. Result presentations were insufficient.) No adverse effects indicated. (J. Christopher, 2/19/85; updated to electronic format Green & Silva, 2/21/03).

TERATOLOGY, RABBIT

** 320 - 086 010236, "H 321: Effects of Oral Administration upon pregnancy in the Rabbit", (Tesh, J.M., Ross, F.W., Secker, R.C., Wilby, O.K., Life Science Research, Stock, Essex, England, Report # 80976, 12/4/81). H 321 (methiocarb, 97.3% pure) was administered by gavage to artificially inseminated New Zealand white female rabbits (17 or 19 rabbits/dose) at 0 (0.5% carboxymethyl cellulose + 0.5% Tween 80), 1, 3 and 10 mg/kg/day on gestation days 6 through 18. Maternal NOEL = 3 mg/kg/day (There was an increase in clinical signs (increased respiratory rate, incoordination, muscular tremors among others) at 10 mg/kg/day). Developmental NOEL = 10 mg/kg/day (There were no treatment-related developmental effects at any dose.) No adverse effects indicated. Acceptable with deficiencies. (J. Christopher, 2/13/85; updated to electronic format, Green & Silva, 2/26/03)

320 - 081 010236 This volume is an exact duplicate of 320 - 086 010236, reviewed above.

TERATOLOGY (dermal), RABBIT

**** 320 - 158, 159 & 160 117877, 122686, 126290** "Embryotoxicity Study (Including Teratogenicity) with H 321 (c.n. Methiocarb) in the Rabbit (Dermal Application)," (Dotti, D.A., Biedermann, K.; RCC, Research and Consulting Company Ltd., Itingen, Switzerland, Report # 103271, 8/6/92; 2 data volumes 320 - 159 & 160 122686 & 126290 contained requested data lacking in the original study). Methiocarb (99.40% pure) was applied dermally (occluded) to shaved backs (10% of total body surface) of mated Chinchilla (CHbb: CH, Hybrids, SPF Quality) rabbits (16/dose) at 0 ("bi-distilled water with 1% Cremophor"), 10, 50 and 250 mg/kg/day from days 6 through 18 of gestation (6 hours/day). Maternal NOEL = 50 mg/kg/day (There was decreased food consumption at 250 mg/kg GD 11 - 15.) Developmental NOEL = 10 mg/kg/day (There were skeletal developmental delays at $\geq$ 50 mg/kg on a per litter basis.) This study, originally reviewed (Green & Silva 2/25/03) as acceptable with a possible adverse effect (skeletal developmental delays on a per litter basis at $\geq$ 50 mg/kg with barely detectable toxicity to dams at 250 mg/kg) did not change in status based on the requested supplemental submissions. (Silva, 3/17/03).

GENE MUTATION

** 320 - 095 010411 "Study of DNA Damage Using the E. coli Pol A$^-$ Test," (Herbold, B.; Bayer AG, Institut Fuer Toxikologie, Wuppertal, Germany, Mobay AgChem #: Report # 85948; Bayer Report #: 11928; 7/13/83). H 321 (methiocarb; 98.6% pure) was used on *Escherichia coli* Pol A- strain (4 cultures/dose) in a DNA damage-repair disc-diffusion assay at 0 (DMSO), 625, 1250, 2500, 5000 and 10000 :g per plate both with and without S9 metabolic activation. Although there were several deficiencies, it was evident that there was no effect resulting from treatment. Acceptable. (J. Christopher, 2/15/85; updated to electronic format, Green & Silva, 3/5/03).

320 - 097 010418 "*Salmonella*/Microscome Test for Determination of Point Mutations" (B. Herbold; Bayer AG, Institut fur Toxikologie, Wuppertal-Elberfeld, Germany, Mobay Report # 67375; Bayer AG Report #: 7978; 12/6/78). H 321 (methiocarb, 98.5% pure) was used on *Salmonella typhimurium* strains TA98, TA100, TA1535 and TA1537 (4 plates/dose/strain) at 0 (DMSO), 4, 20, 100, 500 and 2500 : g/plate with a 48-hour incubation period to test for

histidine reversion. There were no effects due to treatment, however it is uncertain whether or not the positive controls were functioning. Not acceptable and not upgradeable (Treatment without S9 were only at 2500 ug/plate and control. No positive control under non-activated conditions. Also note test article and dosing solution analyses and characteristics and individual data are not included. (J. Schreider, 2/14/85; updated to electronic format, Green & Silva 3/7/03)

** 320 - 130 065934 "*Salmonella*/Microsome Test to Evaluate for Point Mutagenic Effect", (Herbold, D.; Bayer AG, Institute of Toxicology, Wuppertal-Elberfeld, Germany, Report # 91775, 1/10/86). H 321 (methiocarb, 98.4% pure) was tested on *Salmonella typhimurium* strains TA98, TA100, TA1535 and TA1537 at 0 (DMSO), 20.0, 62.5, 100, 125, 250, 500, 1000, 2000, 2500 and 12500 : g/plate both with and without S9 metabolic activation (4 cultures/strain/concentration) for 48 hours. There were no treatment-related increases in gene mutation at any dose or with any strain. Positive controls functioned as expected. No adverse effect. Acceptable. (Green & Silva, 2/26/03).

CHROMOSOME EFFECTS

** 320 - 130 065933 "Sister Chromatid Exchange Assay in Chinese Hamster Ovary (CHO) Cells," (Putman, D.L.; Microbiological Associates, Inc., Bethesda, MD; Report # 91334, 9/25/86). Mesurol technical (97.7% pure) was used on Chinese hamster ovary cells at 0 (untreated), 0 (DMSO), 2, 4, 10, 20, or 40 : g/ml (2 cultures/dose), with and without S9 metabolic activation. Cultures with S9 were treated for 2 hours and those without S9 were treated for 26-32 hours. There was no treatment-related SCE at any dose. Positive controls functioned as expected.. Acceptable. (Green & Silva, 2/26/03)

320 - 097 010417 "Micronucleus Test for Mutagenic Effect on Mice," (B. Herbold, Bayer AG, Institut fur Toxikologie, Wuppertal-Elberfeld, Germany; Bayer Report #: 60939 Mobay Report # 28193, 6/8/79). H 321 (methiocarb; 98.5% pure) was administered by gavage to 4 or 5 NMRI mice (4 - 5/sex/dose) twice, 24 hours apart, at 0 (0.5% Cremophor El), 5, 10, and 20 mg/kg. Adriblastin[å] was used as positive control material. Sampling was performed 6 hours following the second treatment. Positive control functioned as expected. Not acceptable and not upgradeable (Bone marrow sampling occurred early (first sampling at 6 hours, rather than 12 hours) and at only one time point. Excessive toxicity was noted at 20 mg/kg (3/4 M & 2/4 F died). Only 4/sex/dose could be observed at 20 mg/kg. Also, test article and dosing solution analyses and characteristics were not supplied. Observations were not described.). No increase in micronuclei was observed under test conditions. (J. Schreider, 2/14/85; updated to electronic format, Green & Silva, 3/7/03).

320 - 089 010342 "Dominant Lethal Study on Male Mouse to Test for Mutagenic Effects," (Herbold, B.; Bayer AG, Institut fur Toxikologie, Wuppertal-Elberfeld, Germany; Bayer Report #: 8395; Mobay Report # 68129, 5/23/79). H 321 (methiocarb; 98.5% pure) was administered by gavage to NMRI mice (50/males/dose) at 0 (Cremophor EL) and 6 mg/kg. There were 598 and 593 untreated females provided for mating at 0 and 6 mg/kg groups, respectively. Beginning on the day of treatment, a series of twelve 4-day mating periods was performed where each male was caged with one untreated virgin female. At the end of a 4-day period the female was removed and replaced by another. This process was repeated for each of the subsequent mating periods lasting a total of 48 days. A dominant lethal effect was not observed, according to the text, however, the tables were in German, preventing a complete assessment of the data. Not acceptable and not upgradeable (One dosing level was used (rather than 3) and signs/symptoms of toxicity from treatment were absent. There was no positive control. Results were in German only.) No adverse effect indicated. (J. Schreider, 2/13/85; updated to electronic format, Green & Silva, 3/6/03).

320 - 079 944422 This volume is an exact duplicate of 320 - 089 010342, reviewed above.

DNA DAMAGE

** 320 - 143 068777 "Unscheduled DNA Synthesis in Rat Primary Hepatocytes," (Curren, R.D.; Microbiological Associates, Inc., Bethesda and Rockville, MD, Report # 96708, Laboratory Study #: T5391.380; 6/1/88). Mesurol technical (98.8% pure) was used on Sprague-Dawley rat primary hepatocyte cultures (3 cultures/dose) at 0 (untreated), 0 (DMSO), 1 (initial assay only), 3, 10, 30, 45, 60, or 100 :g/ml in an unscheduled DNA synthesis assay by autoradiography (18-20 hours exposure). Twenty-five nuclei/culture were scored for UDS. The release of LDH was used to measure cytotoxicity in parallel with the UDS assay. Female rats were used in the initial assay and males were used in the confirmatory assay. There was no treatment-related unscheduled DNA synthesis observed. No adverse effect indicated. Acceptable. (Green & Silva, 2/28/03)

NEUROTOXICITY

320 - 089 010345 "H 321 (Mesurol Active Ingredient) Neurotoxicity Studies on Hens," (Thyssen, J., Schilde, B.; Bayer AG, Institut Fur Toxikologie, Wuppertal-Elberfeld, Germany, Report # 66482, 6/20/78). H 321 (methiocarb; 98.5% pure) was administered to White Leghorn hens by gavage at 380 mg/kg in 2 doses at a 21 day interval with atropine protection (50 mg/kg). Because of the atropine treatment, the poisoning symptoms, observed after each treatment, were limited to a slight lethargy of brief duration (1 day). After each treatment, 2 H 321-treated hens died. Signs of neurotoxicity (ataxia, paralysis) were not present in methiocarb treated hens. Not acceptable and not upgradeable (Histopathology was incomplete. There was no concurrent vehicle control in the main study and no histopathology for the vehicle control in the preliminary LD50 study. The hens' age (15 to 20 months) was older than guideline specified 8 to 14 months. Bodyweight data was not measured. Test article and dosing solution analyses and characteristics were not presented.) No adverse effect indicated. (J. Schreider, 2/15/85; updated to electronic format, Green & Silva, 3/6/03).

320 - 079 944391 This volume is an exact duplicate of 320 - 089 010345, reviewed above.